Citation:

Oken E, Østerdal ML, Gillman MW, Knudsen VK, Halldorsson TI, Strøm M, Bellinger DC, Hadders-Algra M, Michaelsen KF, Olsen SF. Associations of maternal fish intake during pregnancy and breastfeeding duration with attainment of developmental milestones in early childhood: a study from the Danish National Birth Cohort. *Am J Clin Nutr.* 2008;88(3):789-796.

PubMed ID: 18779297

Study Design:

Prospective Cohort Study

Class:

B - Click here for explanation of classification scheme.

Research Design and Implementation Rating:

POSITIVE: See Research Design and Implementation Criteria Checklist below.

Research Purpose:

To examine associations of maternal fish consumption during pregnancy and the duration of infant breastfeeding with attainment of child developmental milestones reported at 6 and 18 months of age.

Inclusion Criteria:

- Pregnant women enrolled in the Danish National Birth Cohort (DNBC) from 1997 to 2002
- Completed interviews and the food frequency questionnaires (FFQs) during pregnancy and post-partum
- Provided written informed consent

Exclusion Criteria:

Pregnant women past week 12 at recruitment.

Non-singleton pregnancies.

Women who did not have complete data on all previously specified covariates.

Description of Study Protocol:

Recruitment

- General practitioners throughout Denmark recruited 101,042 women at their initial prenatal visit, usually in weeks 6-12 of pregnancy.
- The enrollment in the DNBC from 1997 to 2002 represents 30%of all deliveries in Denmark during these years.

Design: Prospective cohort study

- Enrolled women were instructed to complete computer-assisted telephone interviews at gestation weeks 12 and 30 as well as at 6 and 18 mo after delivery and a self-administered semiquantitative FFQ at gestation week 25.

Blinding used (if applicable): not applicable

Intervention (if applicable): not applicable

Statistical Analysis

- 25,446 children born to mothers participating in the DNBC were included in the data analysis
- ANOVA and Mantel-Haentzel chi-square were used to test for trends across quintiles of fish intake
- Multivariate, cumulative, ordinal and logistic regression analysis for motor, social or cognitive, and total development at 6 and 18 mo were performed to provide single pooled estimate

Data Collection Summary:

Timing of Measurements

- Telephone interview at gestation weeks 12 and 30 and 6 and 18 months after delivery.
- At gestation week 25, a self-administered FFQ was mailed to calculate total fish intake.
- At the 6-mo postpartum interview, mothers reported child development by 13 standardized questions whether the child could hold up his or her head, sit with a straight back, roll back to front, sit unsupported, look in the direction of sounds or voices, throw a toy to the floor, make sounds while playing (other than crying), imitate sounds, reach for objects, crawl, seek contact with the parent (by reaching or making sounds), express dislikes, and bring an object to his or her mouth.
- At the 18-mo postpartum interview, mothers answered 9 standardized questions whether the child could climb stairs, remove his or her socks and shoes, drink from a cup, be occupied for 15 min without adult participation, fetch an object when requested, write or draw, orient a book correctly, use word-like sounds, and put 2 words together.

Dependent Variables

- Developmental milestones at 6 and 18 mo of age

Independent Variables

- Maternal fish intake
- Breastfeeding duration

Control Variables

- Child age, sex, gestation length, and birth weight z score
- Maternal age, marital status, pregnancy BMI, smoking or alcohol use
- Parental education, social status, and learning difficulties

Description of Actual Data Sample:

Initial N: 92,676 women with liveborn singleton infants; 50,276 completed the initial interview

and FFQ; 35,557 completed 6-mo postpartum interview

Attrition: final N=25,446 completed 18-mo postpartum interview

Age: 29.3±4.1 years

Ethnicity: Danish

Other relevant demographics

Anthropometrics

Location: Denmark

Summary of Results:

Key Findings

- 25,446 children were included in data analysis
- Higher maternal fish intake and greater duration of breastfeeding were associated with higher child developmental scores at 18 mo [odds ratio:1.29 (95% CI:1.20, 1.38) for the highest versus the lowest quintile of fish intake, and 1.28 (1.18, 1.38) for breastfeeding for ≥10 mo compared with breastfeeding for ≤1 mo]. Associations were similar for development at 6 mo.
- Associations of fish intake with child development did not differ by breastfeeding duration.

Table 1 Associations of maternal prenatal fish intake [by quintile (Q)] with attainment of developmental milestones at ages 6 mo (*n*=28958) and 18 mo (*n*=25446) among children in the Danish National Birth Cohort

Maternal fish intake (quintiles)	Subject (n)	Median Fish intake (g/d)	Motor development	Social or cognitive development	Total development
6-mo outcomes					
Q1	5744	5.9	1.0 (referent)	1.0 (referent)	1.0 (referent)
Q2	5873	14.5	0.98 (0.92, 1.05)	1.0 (0.93, 1.07)	0.99 (0.92, 1.05)
Q3	5913	22.2	1.03 (0.97, 1.11)	1.07 (0.99, 1.15)	1.05 (0.99, 1.13)
Q4	5823	32.2	1.05 (0.98, 1.12)	1.18 (0.09, 1.27)	1.09 (1.02, 1.17)
Q5	5605	50.8	1.17 (1.09, 1.25)	1.33 (1.23, 1.44)	1.25 (1.17, 1.34)
18-mo outcomes					
Q1	5038	5.9	1.0 (referent)	1.0 (referent)	1.0 (referent)
Q2	5143	14.4	1.00 (0.93, 1.07)	1.00 (0.94, 1.08)	0.99 (0.93, 1.07)
Q3	5117	22.2	1.08 (1.00, 1.16)	1.11 (1.04, 1.19)	1.09 (1.01, 1.17)
Q4	5152	32.3	1.11 (1.03, 1.19)	1.15 (1.07, 1.24)	1.14 (1.06, 1.22)
Q5	4996	50.7	1.24 (1.15, 1.33)	1.28 (1.19, 1.37)	1.29 (1.20, 1.38)

Author Conclusion:

In conclusion, the present study adds to the growing body of evidence that greater maternal fish consumption during pregnancy and a longer duration of breastfeeding are associated with more favorable child development. We support ongoing efforts to promote breastfeeding to optimize a variety of health outcomes, including development. To allow mothers to make the best choices for their children's development, future studies of prenatal diet should incorporate detailed information on fish intake as well as information on both nutrient and toxicant exposures.

Reviewer Comments:

Research Design and Implementation Criteria Checklist: Primary Research

Relevance Questions		
1.	Would implementing the studied intervention or procedure (if found successful) result in improved outcomes for the patients/clients/population group? (Not Applicable for some epidemiological studies)	Yes
2.	Did the authors study an outcome (dependent variable) or topic that the patients/clients/population group would care about?	Yes
3.	Is the focus of the intervention or procedure (independent variable) or topic of study a common issue of concern to nutrition or dietetics practice?	Yes
4.	Is the intervention or procedure feasible? (NA for some epidemiological studies)	Yes
Validity Questions		
1.	**Was the research question clearly stated?**	Yes
1.1.	Was (were) the specific intervention(s) or procedure(s) [independent variable(s)] identified?	Yes
1.2.	Was (were) the outcome(s) [dependent variable(s)] clearly indicated?	Yes
1.3.	Were the target population and setting specified?	Yes
2.	**Was the selection of study subjects/patients free from bias?**	Yes
2.1.	Were inclusion/exclusion criteria specified (e.g., risk, point in disease progression, diagnostic or prognosis criteria), and with sufficient detail and without omitting criteria critical to the study?	Yes
2.2.	Were criteria applied equally to all study groups?	Yes
2.3.	Were health, demographics, and other characteristics of subjects described?	Yes
2.4.	Were the subjects/patients a representative sample of the relevant population?	Yes
3.	**Were study groups comparable?**	Yes
3.1.	Was the method of assigning subjects/patients to groups described and unbiased? (Method of randomization identified if RCT)	Yes
3.2.	Were distribution of disease status, prognostic factors, and other factors (e.g., demographics) similar across study groups at baseline?	Yes

3.3.	Were concurrent controls used? (Concurrent preferred over historical controls.)	N/A
3.4.	If cohort study or cross-sectional study, were groups comparable on important confounding factors and/or were preexisting differences accounted for by using appropriate adjustments in statistical analysis?	Yes
3.5.	If case control or cross-sectional study, were potential confounding factors comparable for cases and controls? (If case series or trial with subjects serving as own control, this criterion is not applicable. Criterion may not be applicable in some cross-sectional studies.)	N/A
3.6.	If diagnostic test, was there an independent blind comparison with an appropriate reference standard (e.g., "gold standard")?	N/A
4.	**Was method of handling withdrawals described?**	Yes
4.1.	Were follow-up methods described and the same for all groups?	Yes
4.2.	Was the number, characteristics of withdrawals (i.e., dropouts, lost to follow up, attrition rate) and/or response rate (cross-sectional studies) described for each group? (Follow up goal for a strong study is 80%.)	Yes
4.3.	Were all enrolled subjects/patients (in the original sample) accounted for?	Yes
4.4.	Were reasons for withdrawals similar across groups?	Yes
4.5.	If diagnostic test, was decision to perform reference test not dependent on results of test under study?	N/A
5.	**Was blinding used to prevent introduction of bias?**	No
5.1.	In intervention study, were subjects, clinicians/practitioners, and investigators blinded to treatment group, as appropriate?	N/A
5.2.	Were data collectors blinded for outcomes assessment? (If outcome is measured using an objective test, such as a lab value, this criterion is assumed to be met.)	N/A
5.3.	In cohort study or cross-sectional study, were measurements of outcomes and risk factors blinded?	No
5.4.	In case control study, was case definition explicit and case ascertainment not influenced by exposure status?	N/A
5.5.	In diagnostic study, were test results blinded to patient history and other test results?	N/A
6.	**Were intervention/therapeutic regimens/exposure factor or procedure and any comparison(s) described in detail? Were interveningfactors described?**	Yes
6.1.	In RCT or other intervention trial, were protocols described for all regimens studied?	N/A

6.2.	In observational study, were interventions, study settings, and clinicians/provider described?	Yes
6.3.	Was the intensity and duration of the intervention or exposure factor sufficient to produce a meaningful effect?	Yes
6.4.	Was the amount of exposure and, if relevant, subject/patient compliance measured?	N/A
6.5.	Were co-interventions (e.g., ancillary treatments, other therapies) described?	N/A
6.6.	Were extra or unplanned treatments described?	N/A
6.7.	Was the information for 6.4, 6.5, and 6.6 assessed the same way for all groups?	N/A
6.8.	In diagnostic study, were details of test administration and replication sufficient?	N/A
7.	**Were outcomes clearly defined and the measurements valid and reliable?**	Yes
7.1.	Were primary and secondary endpoints described and relevant to the question?	Yes
7.2.	Were nutrition measures appropriate to question and outcomes of concern?	Yes
7.3.	Was the period of follow-up long enough for important outcome(s) to occur?	Yes
7.4.	Were the observations and measurements based on standard, valid, and reliable data collection instruments/tests/procedures?	Yes
7.5.	Was the measurement of effect at an appropriate level of precision?	Yes
7.6.	Were other factors accounted for (measured) that could affect outcomes?	Yes
7.7.	Were the measurements conducted consistently across groups?	Yes
8.	**Was the statistical analysis appropriate for the study design and type of outcome indicators?**	Yes
8.1.	Were statistical analyses adequately described and the results reported appropriately?	Yes
8.2.	Were correct statistical tests used and assumptions of test not violated?	Yes
8.3.	Were statistics reported with levels of significance and/or confidence intervals?	Yes
8.4.	Was "intent to treat" analysis of outcomes done (and as appropriate, was there an analysis of outcomes for those maximally exposed or a dose-response analysis)?	N/A
8.5.	Were adequate adjustments made for effects of confounding factors that might have affected the outcomes (e.g., multivariate analyses)?	Yes

8.6.	Was clinical significance as well as statistical significance reported?	Yes
8.7.	If negative findings, was a power calculation reported to address type 2 error?	N/A
9.	**Are conclusions supported by results with biases and limitations taken into consideration?**	Yes
9.1.	Is there a discussion of findings?	Yes
9.2.	Are biases and study limitations identified and discussed?	Yes
10.	**Is bias due to study's funding or sponsorship unlikely?**	Yes
10.1.	Were sources of funding and investigators' affiliations described?	Yes
10.2.	Was the study free from apparent conflict of interest?	Yes